

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 04 AUG 2005

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/NL2005/000205

International filing date (day/month/year)
18.03.2005

Priority date (day/month/year)
18.03.2004

International Patent Classification (IPC) or both national classification and IPC
A61K9/16, A61K38/27

Applicant
OCTOPLUS TECHNOLOGIES B.V.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/NL2005/000205

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/NL2005/000205

Box No. V Reasoned statement under Rule 43*b*/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | |
| | No: Claims | 1-36 |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-36 |
| Industrial applicability (IA) | Yes: Claims | 1-36 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: WO 00/48576 A (UNIVERSITEIT UTRECHT; HENNINK, WILHELMUS, EVERHARDUS; VAN NOSTRUM, COR) 24 August 2000 (2000-08-24)
- D2: CROMMELIN D J A ET AL: "Nanotechnological approaches for the delivery of macromolecules" JOURNAL OF CONTROLLED RELEASE, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 87, no. 1-3, 21 February 2003 (2003-02-21), pages 81-88, XP004412751 ISSN: 0168-3659
- D3: FRANSSEN O ET AL: "Degradable dextran hydrogels: controlled release of a model protein from cylinders and microspheres" JOURNAL OF CONTROLLED RELEASE, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 60, no. 2-3, 5 August 1999 (1999-08-05), pages 211-221, XP004362935 ISSN: 0168-3659
- D4: EP-A-0 842 657 (OCTOPLUS B V) 20 May 1998 (1998-05-20)
- D5: WO 98/00170 A (UNIVERSITEIT UTRECHT; HENNINK, WILHELMUS, EVERHARDUS; VAN DIJK-WOLTHUI) 8 January 1998 (1998-01-08)
- D6: US-B1-6 395 302 (HENNINK WILHELMUS EVERHARDUS ET AL) 28 May 2002 (2002-05-28)

The present application discloses emulsion-based method for the preparation of controlled release microspheres for the delivery of active compounds. the method comprises the preparation of an emulsion comprising an aqueous dispersed phase which comprises a polymer capable of forming a hydrogel, a bioactive protein, and water, and which is substantially free from insoluble aggregates of said bioactive protein. Subsequently, the polymer is physically or chemically crosslinked to form a hydrogel. furthermore, the protein-loaded microspheres which are prepared by said process is disclosed. said microspheres exhibit controlled release properties.

1. Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-36 is not new in the sense of Article 33(2) PCT.

The documents **D1-D6** all disclose (citations see ISR) method for the preparation of controlled release microspheres for the delivery of active compounds. the method comprises the preparation of an emulsion comprising an aqueous dispersed phase which comprises a polymer capable of forming a hydrogel, a bioactive protein, and water, and which is substantially free from insoluble aggregates of said bioactive protein. Subsequently, the polymer is physically or chemically crosslinked to form a hydrogel. furthermore, the protein-loaded microspheres which are prepared by said process is disclosed. said microspheres exhibit controlled release properties.

2. Inventive step

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-36 does not involve an inventive step in the sense of Article 33(3) PCT.

Should the applicant overcome the abovementioned novelty objections, he should turn his attention to the relevance of **D1-D6** with regard to the inventive step of the claimed subject-matter.

3. Industrial applicability

The subject-matter of claims 1-36 seems to be industrial applicable.